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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

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(54) Title: 8-(BIARYL) QUINOLINE PDE4 INHIBITORS

(57) Abstract: 8-(biaryl) quinolines wherein the bi-aryl group at the 8-position is in a *meta* relationship to the quinoline group, are PDE4 inhibitors useful in the treatment of asthma, chronic bronchitis, chronic obstructive pulmonary disease, eosinophilic granuloma, psoriasis and other benign or malignant proliferative skin diseases, endotoxic shock, laminitis in horses, colic in horses, septic shock, ulcerative colitis, Crohn's disease, reperfusion injury of the myocardium and brain, inflammatory arthritis, chronic glomerulonephritis, atopic dermatitis, urticaria, adult respiratory distress syndrome, chronic obstructive pulmonary disease in animals, diabetes insipidus, allergic rhinitis, allergic conjunctivitis, vernal conjunctivitis, arterial restenosis, orthosclerosis, atherosclerosis, neurogenic inflammation, pain, cough, rheumatoid arthritis, ankylosing spondylitis, transplant rejection, graft versus host disease, hypersecretion of gastric acid, bacterial, fungal induced sepsis, viral induced sepsis, fungal induced septic shock, viral induced septic shock, inflammation-mediated chronic tissue degeneration, cytokine-mediated chronic tissue degeneration, osteoarthritis, cancer, cachexia, muscle wasting, depression, memory impairment, tumour growth, or cancerous invasion of normal tissues. In another aspect, the present invention is directed to a method of enhancing cognition in a healthy subject comprising administering a safe cognition enhancing amount of phosphodiesterase-4 inhibitor. In particular, this invention is directed to a method of enhancing memory, learning, retention, recall, awareness and judgement in health subjects comprising administering a safe and cognition enhancing amount of a phosphodiesterase-4 inhibitor.

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INTERNATIONAL SEARCH REPORT

International Application No
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A. CLASSIFICATION OF SUBJECT MATTER

IPC 7	C07D215/04	C07D215/12	C07D409/10	C07D407/10	C07D401/10
	C07D413/10	C07D413/14	C07D471/04	C07D401/04	C07D403/10
	C07D417/10	A61K31/4709	A61K31/47	A61K31/497	A61P29/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category ^a	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5 455 252 A (WILHELM ET. AL.) 3 October 1995 (1995-10-03) column 14, line 25 - line 46; claims; examples ---	1-35
Y	US 5 530 005 A (WILHELM ET. AL.) 25 June 1996 (1996-06-25) column 13, line 35 - line 53; claims; examples ---	1-35
P, Y	WO 02 094823 A (MERCK FROSST CANADA) 28 November 2002 (2002-11-28) page 1, line 5 -page 4, line 16; claims; examples ---	1-35 -/-

 Further documents are listed in the continuation of box C. Patent family members are listed in annex.

° Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the International filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

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Helps, I

INTERNATIONAL SEARCH REPORT

International Application No

PCT/CA 03/00957

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 6 069 151 A (DYKE ET. AL.) 30 May 2000 (2000-05-30) column 4, line 66 -column 5, line 23; claims; examples -----	1-35
A	D. MACDONALD ET. AL.: "Hunting the Emesis and Efficacy targets of PDE4 Inhibitors. Identification of the Photoaffinity Probe 8-(3-Azidophenyl)-6-'(4-Iodo-1H-1-imidazol yl)methyl!quinoline (APIIMQ)" JOURNAL OF MEDICINAL CHEMISTRY, vol. 43, no. 21, 30 September 2000 (2000-09-30), pages 3820-3, XP002254693 table 1 -----	1-35

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA 03/00957

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 25-31 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP A 03/00957

Patent document cited in search report		Publication date		Patent family member(s)	Publication date
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US 6069151	A	30-05-2000		AT 246184 T AU 711587 B2 AU 4875897 A DE 69723863 D1 EP 0946541 A1 WO 9820007 A1 JP 2001503756 T ZA 9710000 A AU 735573 B2 AU 8222898 A CN 1260784 T EP 0993449 A1 WO 9857936 A1 JP 2002504925 T ZA 9805253 A	15-08-2003 14-10-1999 29-05-1998 04-09-2003 06-10-1999 14-05-1998 21-03-2001 06-11-1998 12-07-2001 04-01-1999 19-07-2000 19-04-2000 23-12-1998 12-02-2002 17-06-1999